

III. Remarks

A. Amendments To The Claims

Claim 14 has been amended to correct formal errors.

B. Inventorship

The Examiner has made the following observation about inventorship:

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicants confirm that as of the invention dates of claims 8–21, the subject matter of claims 8–21 was commonly owned. The ownership of the subject matter of claims 8–21 has not changed since the invention thereof.

C. Rejection Under 35 U.S.C. § 103

The Examiner has rejected the pending claims 8–21 under 35 U.S.C. § 103(a) as being unpatentable over S. Zhang and K. E. Gonsalves, J Mater Sci Mater, Med. 8 (1997) 25. (S. Zhang et al. publication) in view of United States Patent No. 5,741,773 to Y. P. Zhang et al. (Y. P. Zhang et al. patent).

1. The Examiner's Reasons for the Rejection

The Examiner's reasons for the rejection are as follows:

Regarding claim 8, Zhang et al. teach a solution (see Experimental procedures) comprising rod-like shaped hydroxyapatite particles having a length of 25 nm (see page 26 second col), wherein the hydroxyapatite crystallizes into hexagonal rhombic prisms (see Introduction) and polyacrylic acid (see page 25 Experimental Procedures section which recites "the starting precipitates without polyacrylic acid were prepared in a similar way" which teaches that the method described includes salt precipitates with polyacrylic acid. See

also Figure 1, which is a micrograph of rod-like hydroxyapatite crystals with polyacrylic acid in the system) to which the calcium is bonded (see page 28). Regarding claim 11, Zhang et al. also teach a method of making rod-like shaped hydroxyapatite particles comprising a 30 ml solution in which 7.63g of calcium nitrite was dissolved and 2 g of polyacrylic acid (2 g of polyacrylic acid is at least .01% of the solution and not greater than 10% absent evidence to the contrary) was added (see Experimental procedures) such that the precipitated hydroxyapatite products were deagglomerated as shown in Figure 1.

Zhang et al. do not teach a solution in which the hydroxyapatite is present in an amount of from 1 to 40% or a toothpaste comprising same nor does Zhang et al. teach gelatin as a specific protective colloid. Nonetheless, Zhang et al. teach polyacrylic acid which according to the instant Specification on page 7 is an equivalent to gelatin as now claimed and absent evidence to the contrary or evidence that the gelatin was identified for particular reasons over other disclosed protective colloids, one of ordinary skill in the art would have appreciated the use of polyacrylic acid in light of the teachings in the instant Specification.

In addition to the teachings in Zhang et al. the '773 Zhang et al. reference teaches hydroxyapatite compositions which include gelatin as a stabilizer (in current claims 15–21; see col 7 lines 15 and 55–65 as well as col 1 lines 40–50).

One of ordinary skill in the art would have been motivated to combine the above references and as combined teach the claimed invention as claimed. One of ordinary skill in the art would have been motivated to combine Zhang et al. with Zhang et al. because both are directed to hydroxyapatite compositions for use as a dentifrice. Moreover, the protective colloids used in each perform the same functions i.e. the polyacrylic acid was used to modify the surfaces and promote calcium carbonate crystal growth whereas the gelatin is used as a stabilizer as well (see col 7 lines 12–15) which are also taught to have antiplaque and anticaries performance (see col 1 lines 42–50). Thus, the combined references teach and make prima facie obvious how to use the claimed invention at the time that it was made.

(Examiner's Action, page 3, line 12 to page 5, line 2).

**2. Comparison between the Subject Matter of the Claims
and the References**

Applicants submit herewith as EXHIBIT A the Declaration of Christian Kropf, one of the inventors of United States Patent Application No. 09/868,379, in support of the arguments made herebelow.

Claim 8 of the Kropf application is directed to a suspension. The remaining claims 9–21 are directed to a process of preparing the suspension, a method of remineralizing teeth, toothpaste comprising the suspension, or other suspensions, all of which comprise the suspension of claim 8 or a more narrowly defined suspension. Claim 8 reads as follows:

A suspension of one or more phosphate calcium salts, fluoride calcium salts or fluorophosphate calcium salts in a liquid medium in which the salts are less than 1 g/l soluble, wherein the calcium salts comprise primary particles having diameters of from 5 to 50 nanometers and lengths of from 10 to 150 nanometers, stabilized against agglomeration by a content of at least 0.01% by weight, based on the weight of the suspension, of a water-soluble surfactant or of a natural water soluble polymeric protective colloid selected from the group consisting of gelatin, casein, albumin, starch, plant gums, water-soluble derivatives of water-insoluble natural polymeric substances, cellulose esters, methylcellulose, hydroxyethylcellulose, carboxymethylcellulose, hydroxyethylstarch and hydroxypropyl guar, adsorbed onto said particles.

Claims 8–21 comprise, *inter alia*, a suspension of one or more calcium salts in a liquid medium. The calcium salts comprise primary particles having diameters of from 5 to 50 nanometers and lengths of from 10 to 150 nanometers. The particles are stabilized against agglomeration by a content of at least 0.01% by weight of a water-soluble surfactant or of a natural water-soluble polymeric protective colloid selected from a defined group of colloids. The surfactant or colloid is adsorbed onto said particles.

As noted above, the Examiner relies on the S. Zhang et al. publication as teaching a solution comprising rod-like shape hydroxyapatite particles having a length of 25 nm, wherein the hydroxyapatite crystallizes into hexagonal rhombic prisms, as well as polyacrylic acid. Polyacrylic acid is defined in the specification at page 7, lines 14–17 as a synthetic colloid.

The S. Zhang publication discloses a new method of preparing thermally stable, pure, rod-like HAp (hydroxyapatite) particles. (Page 25, first column, lines 25–28). According to the method disclosed in the S. Zhang publication, polyacrylic acid is added to a solution to obtain

a precipitation of particles of pure hydroxyapatite, instead of particles comprising both hydroxyapatite and tricalcium phosphate. This reason for using a solution comprising polyacrylic acid in Zhang's method of preparing pure hydroxyapatite particles is disclosed, for example, in the S. Zhang publication in the following passage bridging pages 26 and 27:

A pure HAp well-crystallized structure (Fig. 2e, SH-2) is obtained from the system containing polyacrylic acid and treated hydrothermally. A well-crystallized structure is also observed in the sample S-2, however, it is a mixture of TCP (tricalcium phosphate) and HAp (Fig. 2d, S-2). **Therefore, hydrothermal treatment and polyacrylic acid addition stabilized the synthetic hydroxyapatite.** (emphasis added).

This purpose for using polyacrylic acid is also illustrated by the following statement in the S. Zhang publication bridging pages 27–28:

Fig. 4a is a typical XPS core spectrum for Ca2p which has 2 peaks separated by 3.5 eV in bonding energy. Another calcium peak appeared at low binding energy, with area approximately 20% of the total calcium element, which matches the amount of PAA added. This calcium is bonded to polyacrylic acid [13, 14]. A weight loss of 20% also appeared in the TGA curve in the temperature range 300–400°C. **The detailed mechanism of how the polyacrylic acid stabilizes the hydroxyapatite during calcining up to 1100°C is under further investigation.** (emphasis added).

(Declaration of Christian Kropf, Paragraph 5).

The S. Zhang publication also discloses a process of obtaining precipitated HAp, not a suspension of HAp in a liquid. The precipitated HAp produced according to the process disclosed in the S. Zhang publication is in the form of particles consisting of rod-like crystals. (Fig. 1 and page 26, second column, lines 1–8). (Declaration of Christian Kropf, Paragraph 6).

In the S. Zhang publication, the statement in the caption of Fig. 1 and in the last sentence of column 1, page 26: "Here 1 represents the system without polyacrylic acid and 2 the system with polyacrylic acid in the starting precipitates" refers to hydrothermally treated precipitates which were made with solutions containing the starting materials with or without polyacrylic acid. Figs. 1(a) and (b) are identified as showing "TEM photographs of rod-like crystals of HAp after hydrothermal treatment: (a) without polyacrylic acid (H-1); and (b) with polyacrylic acid in the system (H-2)." The "TEM" (transmission electron microscope, operated under high vacuum conditions) photographs show precipitated and hydrothermally treated crystalline particles of HAp arranged on a metal grid (typically copper or nickel) with an

amorphous carbon or formvar[®] layer as a specimen carrier, and do not show Applicants' claimed suspension comprising calcium salt nanoparticles in a liquid. (Declaration of Christian Kropf, Paragraph 7).

The S. Zhang publication also discloses that the particles precipitated in the solution comprising polyacrylic acid, which is a synthetic colloid, produce poorly crystallized apatite structures. Such poorly crystallized apatite structures must be further treated hydrothermally and then sintered or calcined at 1,100°C for two hours to make pure HAp well-crystallized particles. (Page 26, second column, line 19, to page 27, column 1, line 1). These HAp particles contain no polyacrylic acid because all polyacrylic acid that was present in the system used to prepare the precipitated HAp particles is decomposed and evaporated during the calcining step. The pure HAp is shown by SH-2 in Figs. 2(f) and 3. (Declaration of Christian Kropf, Paragraph 8).

The calcium particles claimed in claim 8 of the Kropf application are not pure HAp. They are particles of calcium salt with a colloid selected from a group of natural colloids adsorbed onto said particles. Accordingly, the particles claimed in the Kropf application are different in composition than the pure HAp particles produced after the sintering process step disclosed by the S. Zhang publication. (Declaration of Christian Kropf, Paragraph 9).

The S. Zhang et al. publication discloses a "new method of preparing thermally stable rod-like HAp. (Page 25, lines 27–28). In the Zhang et al. publication, "pure and thermally stable HAp was obtained by adding low molecular weight polyacrylic acid into calcium nitrate and ammonium dibase phosphate, followed by hydrothermal treatment" (sentence bridging columns of page 25). According to the S. Zhang et al. publication:

The starting precipitates, both with and without polyacrylic acid, have poorly crystallized apatite structure. . . . After calcining the starting precipitates at 1100°C for two h. [hours], the difference in XRD patterns between the two systems is obvious. A pure HAp [hydroxyapatite] well-crystallized structure (Fig. 2e, SH-2) is obtained from the system containing polyacrylic acid and treated hydrothermally. A well-crystallized structure is also observed in the sample S-2, however, it is a mixture of TCP (tricalcium phosphate) and HAp (Fig. 2d, S-2). Therefore, hydrothermal treatment and polyacrylic acid addition stabilized the synthetic hydroxyapatite.

(Paragraph bridging pages 26–27).

Fig. 3 indicates that SH-2 has 100% HAp and 0% TCP, whereas S-2 has approximately 90% HAp to 10% TCP. The Y. P. Zhang et al. patent is not relied on by the Examiner as disclosing, and does not disclose, calcium salts comprising primary particles having diameters of 5 to 50 nanometers and lengths of 10 to 150 nanometers. The Y. P. Zhang et al. patent also does not disclose nanoparticles in which a surfactant or colloid is adsorbed onto the particles.

3. There is no *Prima Facie* Case of Obviousness Warranting Rejection of Claims 8–21 Under 35 U.S.C. § 103(a) as Unpatentable over the Combination of the Prior Art

(i) All claim limitations are not taught or suggested by the references.

Section 2143 of the Manual of Patent Examining Procedure states that “in order to establish a *prima facie* case of obviousness. . . . the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not be based on applicant’s disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).”

A comparison of the limitations set forth in claim 8 with the subject matter disclosed in the S. Zhang publication reveals that the claimed suspension is not taught or suggested by the S. Zhang publication. The S. Zhang publication discloses the production of particles of pure HAp, or a mixture of HAp and TCP (tricalcium phosphate) (as shown in Fig. 3). Accordingly, the S. Zhang particles are therefore distinct from Applicants’ claimed particles of calcium salt, wherein a natural water-soluble polymeric protective colloid is adsorbed onto said particles. The Y.P. Zhang patent does not disclose calcium salt particles in the form of nanoparticles. Accordingly, the S. Zhang publication and the Y.P. Zhang patent do not disclose or suggest Applicants’ claimed suspension comprising particles of calcium salt with a colloid adsorbed onto said particles, which is set forth in all of Applicants’ pending claims 8–21. (Declaration of Christian Kropf, Paragraph 10).

Hence, the claimed suspension of particles onto which is adsorbed a water-soluble surfactant or colloid are different in composition than the pure HAp particles obtained according to the process of the S. Zhang et al. publication. A modification of the process set forth in the S. Zhang et al. publication cannot disclose to one of ordinary skill in the art, Applicants’ claimed

particles as S. Zhang et al. employs a synthetic colloid only in the production of pure hydroxyapatite. Applicants' claimed suspension of particles have adsorbed onto the particles a water-soluble surfactant or natural colloid.

The Y. P. Zhang et al. patent does not disclose the production of nanoparticles, let alone nanoparticles onto which is adsorbed a water-soluble surfactant or natural colloid.

**(ii) Prior art must be considered in its entirety,
including disclosures that teach away from the claims.**

A prior art reference must be considered in its entirety, *i.e.*, as a **whole**, including portions that would lead away from the claimed invention. *W. L. Gore and Associates, Inc., v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984) (MPEP 2141.02).

If the Y. P. Zhang et al. patent and the S. Zhang et al. publication are considered in their entireties, including disclosures that teach away from the claims, the Y. P. Zhang et al. patent teaches away from the claimed suspension of calcium particles in the form of nanoparticles in a liquid. The Y. P. Zhang et al. patent does not even disclose nanoparticles. The S. Zhang et al. publication discloses the production of solids of pure rod-like HAp or a mixture of HAp and TCP (as shown in Fig. 3), which is distinct from Applicants' claimed particles of calcium salt, wherein a polymeric protective surfactant or natural water-soluble colloid is adsorbed onto said particles. The Y.P. Zhang et al. patent and the S. Zhang et al. publication therefore fail to disclose and thus teach away from Applicants' claimed suspension. (Declaration of Christian Kropf, Paragraph 11).

**(iii) A proposed modification cannot render prior art
unsatisfactory for its intended purpose.**

If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). (MPEP Section 2143.01).

The purpose of the process disclosed in the S. Zhang et al. publication is to prepare **pure** and thermally stable HAp (*emphasis added*). Eliminating the sintering step from the

process disclosed in the S. Zhang et al. publication to try to incorporate polyacrylic acid onto the HAp particles renders the process unsatisfactory for its purpose of creating pure crystalline hydroxyapatite particles. (Declaration of Christian Kropf, Paragraph 12).

**(iv) A proposed modification cannot change the principle
of operation of a reference.**

If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the reference are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

The principle of operation of the S. Zhang et al. publication is the production of precipitated solids of pure HAp (as shown in Fig. 3). Accordingly, the particles are distinct from Applicants' claimed suspension comprising particles of calcium salt, wherein a natural water-soluble polymeric protective colloid is adsorbed onto said particles. A modification of the process disclosed in the S. Zhang et al. publication, eliminating the hydrothermal and sintering treatment steps in an effort to try to obtain Applicants' claimed suspension, would change the principle of operation of the reference as that step is required by S. Zhang to obtain pure HAp well-crystallized particles. (Declaration of Christian Kropf, Paragraph 13).

Accordingly, for the reasons set forth above, the rejection of claims 8–21 under 35 U.S.C. as unpatentable over the S. Zhang et al. publication and the Y. P. Zhang et al. patent, is untenable and should be withdrawn.

D. Double Patenting Rejection

Claims 8–14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 21 of co-pending United States Patent Application No. 10/297,842 in view of the Y. P. Zhang et al. patent.

Applicants submit herewith as **EXHIBIT B** a Terminal Disclaimer of the term of any patent issuing from the present application beyond the complete term of any patent arising from United States Patent No. 10/297,842. With the filing of the Terminal Disclaimer, the rejection of claims 8–14 is believed to have been overcome and should be withdrawn.

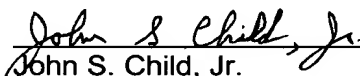
IV. Conclusion

It is believed that the above Amendment and Remarks constitute a complete response under 37 CFR § 1.111 and that all bases of rejection in the Examiner's Action have been adequately rebutted or overcome. A Notice of Allowance in the next Office Action is, therefore, respectfully requested. The Examiner is requested to telephone the undersigned attorney if any matter that can be expected to be resolved in a telephone interview is believed to impede the allowance of pending claims 8–21 of United States Patent Application Serial No. 09/868,379.

Respectfully submitted,

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